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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/626,096	07/26/2000	Robert M Umek	067456-5030-US	8157

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EXAMINER

CALAMITA, HEATHER

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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02/07/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/626,096

Applicant(s)

UMEK ET AL.

Examiner

Heather G. Calamita, Ph.D.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 60-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 60-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 12, 2007, has been entered.

Status of Application, Amendments, and/or Claims

2. Claims 60-69 are currently pending and under examination. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 60-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kayyem et al. (WO 98/20162) in view of Shuber (USPN 5,633,134).

With regard to claim 60, Kayyem et al. teach a method of determining the identification of nucleotide(s) at a first detection position in a first domain of a target sequence, said target sequence comprising said first domain and a second domain, said method comprising:

- a. providing an electrode with a covalently attached capture probe, wherein said capture probe has a sequence substantially complementary to said second domain of said target sequence (see p. 36 lines 10-22)
- b. contacting said electrode with:
 - (i) said target sequence;
 - (ii) a first label probe substantially complementary to said first domain, comprising a first nucleotide at an interrogation position and a first electron transfer moiety (ETM) with a first redox potential (see p. 36 lines 10-22);

With regard to claim 63, Kayyem et al. teach an array of capture probes (see p. 36 lines 10-14, where the plurality of oligomers attached to a plurality of nucleic acids on a plurality of electrodes comprises the array).

With regard to claim 64, Kayyem et al. teach the first label probes contains a plurality of first ETMs (see p.36 lines 30-32).

With regard to claims 66-69, Kayyem et al. teach a ferrocene derivative (see p.41 line 21-24, where a substituted ferrocene is a ferrocene derivative and a transition metal ETM).

Kayyem et al. do not teach step (iii) a second label probe complementary to the first domain comprising a second nucleotide at said interrogation position.

With regard to claim 61, Kayyem et al. do not teach a third label probe complementary to the first domain comprising a third nucleotide at said interrogation position.

With regard to claim 62, Kayyem et al. do not teach a fourth label probe complementary to the first target domain comprising a fourth nucleotide at said interrogation position.

Shuber teaches allele specific oligonucleotide hybridization using allele specific oligonucleotide probes.

With regard to claim 60, Shuber teaches multiple oligonucleotide probes with labels for determining nucleotides at the detection position (see abstract and col. 5 lines 13-21 and table 1, where the ASO are the labeled probes used to detect the mutations at the interrogation position)

With regard to claims 62 and 65, Shuber teach multiple probes (see col. 5 table 1, which comprises the multiple labeled probes).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the ETM labeled oligonucleotides, as taught by Kayyem et al. with the multiple oligonucleotide probes for mutation detection, as taught by Shuber since Kayyem states, "In general electron transfer between electron donors and acceptors does not occur at an appreciable rate when the nucleic acid is single stranded, nor does it occur appreciably unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor in the double helical structure (see p. 9 lines 21-24)." An ordinary practitioner would have been motivated to use ETM labeled oligonucleotides, as taught by Kayyem et al. with the multiple oligonucleotide probes for mutation detection because Kayyem states that no electron transfer occurs unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor. This property is particularly advantageous for the detection of nucleotide mutations using the multiple probe methods as describe by Shuber in allele specific oligonulceotide hybridization.

Response to Arguments

3. Applicants' arguments with respect to the rejections over Kayyem and Schuber have been fully considered but they are not persuasive.

Applicants argue that Shuber teaches a two step method to detect multiple mutations in one or more genes simultaneously. Applicants argue that when Shuber uses multiple probes Shuber does not determine the nucleotide at a particular position but an individual reaction is required to determine which mutation is present. Therefore Shuber does not teach a second label probe comprising a second ETM with a second redox potential. This argument is not persuasive because Shuber teaches detection of a mutation using multiple probes. Shuber teaches a first step using multiple probes and if a positive result is present then in a second step a second probe is used to determine which mutation is present. The claims recite the open language of comprising and therefore the additional reaction required by Shuber to determine which mutation is present is permitted.

Applicants argue Shuber teaches using the same label for the probes. This argument is not persuasive because Shuber teaches multiple labels which can be used for detection. Additionally Kayyem teaches a first ETM label on a first oligonucleotide and a second ETM label on a second oligonucleotide where upon hybridization an electron is transferred from one ETM on the first oligonucleotide to the second ETM on the second oligonucleotide (see p. 52 lines 6-24).

Applicants argue Shuber does not teach multiple probes to interrogate the same detection position. This argument is not persuasive because claim 60 requires only that the probes are complementary to the same domain and Shuber teaches ASO probes which are used to detect mutations at multiple interrogation positions. The interrogation position of Shuber is the base which basepairs with the detection position and in Shuber there are multiple detection positions. Moreover in lines 13-14 of the instant specification indicate the detection position may comprise a plurality of nucleotides...either contiguous or separated and at p. 12 line 13-14 state the interrogation position is the base which base pairs with the detection position and as described in the specification the detection position may comprise a plurality of nucleotides...either contiguous or separated. Therefore the probes of Shuber meet the limitation of claim 60 in that Shuber teaches multiple oligonucleotide probes specific for one domain and

this is the only requirement of the claim. Shuber teach multiple oligonucleotide probes with labels for determining nucleotides at the detection position at col. 5 lines 13-21. Here Shuber describes ASOs (labeled probes) which are used to detect mutations at multiple interrogation positions. Shuber teaches the probes are complementary to different mutations sites of the same gene or same sequence. According to the instant specification multiple detection positions are permitted.

Applicants argue there is no motivation to combine the teachings of the references because Shuber teaches away from the claimed invention. This argument is not persuasive because while the method of Shuber is a two step method that alone does not lead a skilled artisan away from using multiple and different labels. As outlined in the rejection above, Kayyem states that no electron transfer occurs unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor. This property is particularly advantageous for the detection of nucleotide mutations using the multiple probe methods as describe by Shuber in allele specific oligonulceotide hybridization. Therefore a skilled artisan would want to apply the ETM labels as taught by Kayyem with the multiple probes taught by Shuber to have a more efficient and accurate detection method.

Summary

4. No claims allowed.

Conclusion

5. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a

request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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